	NUMBER	DATE
PRIORITY INFORMATION:	GB 1975-19144	19750507
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Roberts, Elbert L.	
LEGAL REPRESENTATIVE:	McFadden, Fincham & Co.	
NUMBER OF CLAIMS:	51	
EXEMPLARY CLAIM:	1,3	
LINE COUNT:	2665	

=>

SUMM . . . with only slight respiratory inhibition. Due to these pharmacological properties, the adverse effects associated with the narcotic analgesics have greatly **improved**. They decrease the incidence of addiction and diminish the inhibitory effect on the respiratory system. Shafer, S. L. et al.. . .

SUMM Nalbuphine has been found to be **effective** in control of severe and deep pain caused by cardiac, pulmonary, abdominal, osteopathia, and obstetrical surgery, severe burn injury and. . . of action. Wang, J. J. et al. (Ma. Tsui. Hsueh. Tsa. Chi., Vol 23, 3, 1985) have reported that the **effect** of nalbuphine can only be sustained for 3-5 hours after intravenous administration and 6-8 hours by intrathecal injection. However, severe. . .

SUMM Therefore, any **improvement** in extending the duration of action of nalbuphine would be a great breakthrough in medicine and at the same time would provide a more economical therapeutic system. The prodrug approach is widely used to **increase** the duration of drugs that are rapidly eliminated. The antipsychosis agent, haloperidol, is one example. Hemstrom, C. A. et al.. . . haloperidol decanoate can be prolonged from 2-4 times a day to 1-2 times a month. Joshi, J. V. et al. (**Steroids**, Vol. 53, 571, 1989) also reported that the prodrug of northisterone enanthate can be given once every 2 months.

SUMM . . . long-acting mechanism of action of ester-type prodrugs. They are esterified with fatty acids of different carbon numbers resulting in an **increase** in lipophilicity of the prodrugs. Therefore, when prodrugs are given intramuscularly, the release rates are decreased and the duration of action is prolonged. Ester-type prodrugs are **hydrolyzed** by **esterases** in the body resulting in the **increase** of the mother compounds. Esterase exists in many tissues and organs, such as blood, brain, liver, heart, lungs, kidneys, and muscles. The pharmacological **effect** and safety of the ester-type prodrug and the mother compound are reported to be the same (Gelders, Y. G. et. . .

L5 ANSWER 1 OF 6 USPATFULL

ACCESSION NUMBER:	1998:51610 USPATFULL
TITLE:	Nalbuphine esters having long acting analgesic action and method of use
INVENTOR(S):	Yoa-Pu, Hu Oliver, Taipei, Taiwan, Province of China Wang, Jhi-Joung, Taipei, Taiwan, Province of China Shung-Tai, Ho, Taipei, Taiwan, Province of China
PATENT ASSIGNEE(S):	National Science Council, Taipei, Taiwan, Province of China (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5750534		19980512
APPLICATION INFO.:	US 1996-690361		19960726 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-161257, filed on 16 Mar 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Jarvis, William R. A.		
LEGAL REPRESENTATIVE:	Bucknam and Archer		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	35 Drawing Figure(s); 35 Drawing Page(s)		
LINE COUNT:	659		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L26 ANSWER 14 OF 53 USPATFULL

ACCESSION NUMBER:	2000:91955 USPATFULL
TITLE:	Lipid soluble steroid prodrugs
INVENTOR(S):	Unger, Evan C., Tucson, AZ, United States Shen, DeKang, Tucson, AZ, United States
PATENT ASSIGNEE(S):	Imarx Pharmaceutical Corp., Tucson, AZ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6090800		20000718
APPLICATION INFO.:	US 1997-851780		19970506 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Dees, Jose' G.
ASSISTANT EXAMINER:	Badio, Barbara
LEGAL REPRESENTATIVE:	Woodcock Washburn Kurtz Mackiewicz & Norris LLP
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
LINE COUNT:	6285

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

L15 ANSWER 2 OF 7 USPATFULL
AN 2000:98413 USPATFULL
PI US 6096728 20000801
IN Collins, David S., Lafayette, CO, United States
Bevilacqua, Michael P., Boulder, CO, United States

L15 ANSWER 3 OF 7 USPATFULL
AN 1999:4658 USPATFULL
PI US 5859001 19990112
IN Simpkins, James W, Gainesville, FL, United States
Gordon, Katherine, Winchester, MA, United States
Green, Pattie S., Gainesville, FL, United States

L5 ANSWER 29 OF 33 USPATFULL

ACCESSION NUMBER:	77:18406 USPATFULL
TITLE:	Propylene carbonate ointment vehicle
INVENTOR(S):	Shastri, Subramaniam, Cupertino, CA, United States Shaikh, Zafaruzzaman I., Palo Alto, CA, United States
PATENT ASSIGNEE(S):	Syntex Corporation, Panama, Panama (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4017615		19770412
APPLICATION INFO.:	US 1975-639740		19751211 (5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1970-85246, filed on 29 Oct 1970, now abandoned		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Roberts, Elbert L.
LEGAL REPRESENTATIVE:	Moran, Tom M., Hirsch, Joseph I.
NUMBER OF CLAIMS:	7
EXEMPLARY CLAIM:	1
LINE COUNT:	570

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

3888998

L5 ANSWER 1 OF 6 USPATFULL

SUMM . . . with only slight respiratory inhibition. Due to these pharmacological properties, the adverse effects associated with the narcotic analgesics have greatly **improved**. They decrease the incidence of addiction and diminish the inhibitory effect on the respiratory system. Shafer, S. L. et al.. . .

SUMM Nalbuphine has been found to be **effective** in control of severe and deep pain caused by cardiac, pulmonary, abdominal, osteopathia, and obstetrical surgery, severe burn injury and. . . of action. Wang, J. J. et al. (Ma. Tsui. Hsueh. Tsa. Chi., Vol 23, 3, 1985) have reported that the **effect** of nalbuphine can only be sustained for 3-5 hours after intravenous administration and 6-8 hours by intrathecal injection. However, severe. . .

SUMM Therefore, any **improvement** in extending the duration of action of nalbuphine would be a great breakthrough in medicine and at the same time would provide a more economical therapeutic system. The prodrug approach is widely used to **increase** the duration of drugs that are rapidly eliminated. The antipsychosis agent, haloperidol, is one example. Hemstrom, C. A. et al.. . . haloperidol decanoate can be prolonged from 2-4 times a day to 1-2 times a month. Joshi, J. V. et al. (**Steroids**, Vol. 53, 571, 1989) also reported that the prodrug of northisterone enanthate can be given once every 2 months.

SUMM . . . long-acting mechanism of action of ester-type prodrugs. They are esterified with fatty acids of different carbon numbers resulting in an **increase** in lipophilicity of the prodrugs. Therefore, when prodrugs are given intramuscularly, the release rates are decreased and the duration of action is prolonged. Ester-type prodrugs are **hydrolyzed** by **esterases** in the body resulting in the **increase** of the mother compounds. Esterase exists in many tissues and organs, such as blood, brain, liver, heart, lungs, kidneys, and muscles. The pharmacological **effect** and safety of the ester-type prodrug and the mother compound are reported to be the same (Gelders, Y. G. et. . .

L26 ANSWER 20 OF 53 USPATFULL

DETD The compounds of the present invention are derivatives of various 3.alpha.-hydroxylated-pregnanes and 3.alpha.-hydroxylated -androstanes, and **ester**, ether, sulfonate, sulfate, phosphonate, phosphate, oxime, thiosulfate, heterocyclic and heteroaryl derivatives thereof, and derivatives referred to as **prodrugs**. The expression " **prodrug**" denotes a derivative of a known direct acting drug, which derivative has **enhanced** delivery characteristics and therapeutic value as compared to the drug, and is transformed into the active drug by an enzymatic. . . R. E., Methods in Enzymology, 112:309-323 (1985); Bodor, N., Drugs of the Future, 6(3):165-182 (1981); and Bundgaard, H., "Design of **Prodrugs**: Bioreversible-Derivatives for Various Functional Groups and Chemical Entities," in Design of **Prodrugs**, H. Bundgaard, ed., Elsevier, New York (1985). It should be noted that some of the synthetic derivatives forming part of the present invention may not be true **prodrugs** because, in addition to the above characteristics, they also possess inurinsic activity. However, for purposes of this application they will be referred to as **prodrugs**.

DETD Earlier studies (Gee, K. W. et al., European Journal of Pharmacology, 136:419-423 (1987)) demonstrated that certain 3.alpha.-hydroxylated **steroids** are orders of magnitude more potent as modulators of the GRC than others had reported (Majewska, M. D. et al.,. . . N. L. et al., J. Pharmacol. Exp. Ther. 241:346-353 (1987)). Majewska et al. and Harrison et al. taught that 3.alpha.-hydroxylated-5-reduced **steroids** are only capable of much lower levels of **effectiveness**. In vitro and in vivo experimental data have now demonstrated that the high potency of these **steroids** allows them to be therapeutically useful in the modulation of brain excitability via the GRC (Gee, K. W. et al., European Journal of Pharmacology, 136:419-423 (1987); Wieland et al., Psychopharmacology 118(1):65-71 (1995)). Various synthetic **steroids** have been prepared as neuroactive **steroids**. See, for example, U.S. Pat. No. 5,232,917, issued Aug. 3, 1993, which discloses neuroactive **steroid** compounds useful in treating stress, anxiety, insomnia, seizure disorders and mood disorders that are amenable to GRC-active agents, such as depression, in a therapeutically beneficial manner. Furthermore, it has been previously demonstrated that these **steroids** interact at a unique site on the GRC which is distinct from other known sites of interaction (i.e., barbiturate, BZ, and GABA) where therapeutically beneficial **effects** on stress, anxiety, sleep, mood disorders and seizure disorders have been previously elicited (Gee, K. W. and Yamamura, H. I.,. . .

AN 1999:81822 USPATFULL

PI US 5925630 19990720

TI Neuroactive steroids of the androstane and pregnane series

IN Upasani, Ravindra B., Foothill Ranch, CA, United States
Fick, David B., Mission Viejo, CA, United States
Hogenkamp, Derk J., Carlsbad, CA, United States
Lan, Nancy C., South Pasadena, CA, United States

=>

L28 ANSWER 1 OF 1 USPATFULL

SUMM . . . more simple analogs which still could possess useful biological utility. In these analogs only the C and D-ring of the **steroidal** ring system would be retained and their total synthesis could be a relatively easy task.

SUMM The 19-formate **ester** of 3-deoxycannogenol, though being less active than 3-deoxycannogenol, may be useful as a **"prodrug"**. As it is more lipophilic it may be even more readily absorbed orally than 3-deoxycannogenol, which after absorption of the formate **ester** may then be released by enzymatic hydrolysis. Also the duration of the activity may be favourably prolonged if 3-deoxycannogenol is administered as the formate. Similarly the other **esters** of 3-deoxycannogenol of formula I may be useful as **effective prodrugs**.

SUMM . . . the 19-nor analog of 3-deoxycannogenol lies in the fact that it is the most simple 14.beta.-hydroxy cardenolide with an intact **steroid** ring system which so far has been prepared. Therefore it is well suited as a reference compound for the development of **improved** structure activity relationships and hence is expected to be a useful tool in the design of **improved** cardiotonic compounds. Also containing only functions necessary for cardiotonic activity it may be relatively free of other undesired physiological activities.

SUMM . . . the cardanolides of formula I lies in the observation that the dihydro analogs of cardenolides, though having a reduced inotropic **effect**, exhibit an even more reduced toxicity and hence have a better therapeutic ratio than the unsaturated analogs (see for example. . .

SUMM . . . 7.beta., 8.beta., 9.beta., 10.beta., 11.beta. and 12.beta.-hydroxy 3-deoxy cardenolides of formula I is considered to lie in their ability to **increase** heart-activity. As evident from emerging structure activity relationships, and as has long been recognized for the 19-hydroxy group, polar groups, in particular, hydroxy groups, on the .beta.-side of the steroid molecule **enhance**, while those on the .alpha.-side, e.g. 3.alpha.-hydroxy groups, such as formed by enzymatic epimerization of 3.beta.-hydroxy groups, reduce heart-activity.

DETD . . . S; OCHO), 5.06-5.83 (3, m; 3--H, 4--H, 7--H), 4.53-4.90 (1, m; 17.alpha.--H), 4.21 (2, broadened S; 19--H), 1.20 (9, S; **trimethylacetate**) and 0.70 (3, S; 18--H) ppm m/e 400 (molecular ion), 371, 354 and 398, considered to consist of 19-formyloxy-17.beta.-pivaloxy-5.beta.-androsta-3,7-diene. Tlc. . .

DETD . . . bond in position 3, adjacent to 5,7-cyclopropyl group), 4.67-5.20 (1, m; 20.alpha.--H), 4.23 (2, broadened S; 19--H), 1.20 (9, S; **trimethylacetate**), 1.14 (3, d; 21--H) and 0.87 (3, S; 18--H) ppm, ir (KBr) 3000, 2942, 2918, 2858, 1715, 1470, 1445, 1388,. . .

DETD . . . 4--H, double bond in position 3 adjacent to 5.7-cyclopropyl group?), 4.67-5.17 (1, m; 3.63 (2, dd; 19--H)) 1.20 (9, S, **trimethylacetate**), and 0.83 (3, S; H--18) ppm, m/e 398 (molecular ion), and 297 (m--101).

ACCESSION NUMBER: 78:39280 USPATFULL
TITLE: 14 .beta.-Hydroxy 3-deoxycardenolides
INVENTOR(S): Kruger, Gunther, St. Laurent, Canada
PATENT ASSIGNEE(S): Steele Chemicals Co. Ltd., Pointe Claire, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4102884		19780725	
APPLICATION INFO.:	US 1976-683843		19760505	(5)

trimethylacetate), and 0.83 (3, S; H--18) ppm, m/e 398 (molecular ion), and 297 (m--101).

DETD A mixture of 250 mg of **progesterone**, 7.5 g of zinc dust, 18.75 ml of methylene chloride and 6.25 ml of 90% formic acid was shaken at. . .

PI US 4102884 19780725

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(21) International Application Number: PCT/GB90/01750

(22) International Filing Date: 13 November 1990 (13.11.90)

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8925833.9 15 November 1989 (15.11.89) GB

(71) Applicant *(for all designated States except US)*: ROBERTET S.A. [FR/FR]; 37, avenue Sidi-Brahim, F-06330 Grasse (FR).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)* : BETTS, John, Adrian [GB/GB]; Valhalla, New Road, Haslemere, Surrey GU27 3RW (GB).

(74) Agent: GEE & CO.; Chancery House, Chancery Lane, London WC2A 1QU (GB).

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(54) Title: DERIVATIVES OF AROMATIC BENZOATES AS INHIBITORS OF ESTERASE-PRODUCING MICRO-ORGANISMS

(57) Abstract

Inhibitors of esterase-producing microorganisms comprise, as acitve ingredient, a benzyl or phenyl benzoyloxybenzoate (I) which is hydrolysed by esterases to produce three mononuclear benzene compounds which between them bear at least two hydroxyl and two carboxyl substances, and which impart an anti-microbial action. The inhibitors may be formulated as personal deodorants or dermatological agents.

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DERIVATIVES OF AROMATIC BENZOATES AS INHIBITORS OF ESTERASE-PRODUCING MICRO-ORGANISMS

This invention relates to derivatives of aromatic benzoates as inhibitors of esterase-producing micro-organisms, for use primarily in deodorant compositions.

The human skin has a large natural population of micro-organisms. These organisms are nourished by various skin-secreted substances, skin cell debris, breakdown products of the skin and the organisms themselves. The skin secretions are conveniently divided into two groups, those containing water-soluble materials and constituted by eccrine and apocrine sweat, and sebum which contains lipid-soluble materials. These secretions will be referred to as 'liquid body-secretions' and they will now be described, as will their functions as they are generally understood.

Eccrine sweat consists mainly of a watery solution of dissolved salts and is produced by glands distributed over the whole skin surface. In conditions of occlusion, e.g. feet enclosed in socks and shoes, the eccrine sweat accumulates, and in these warm damp conditions, the skin debris, together with nutrients from the sweat, provide a medium for micro-organism growth with the

possibility of massive overgrowth of one type. This can result, in the first instance, in odorous metabolic products, and in the second, in clinical infection with maceration of the skin and irritation.

Apocrine sweat is produced by the apocrine glands at specific sites on the body, notably the axillae, the anogenital area and around the nipples. Although present at birth, the apocrine glands are not functional until puberty when they are influenced by circulating androgens. Apocrine secretion differs from eccrine sweat in containing lipids (fatty materials) and proteins. In the warm, damp occlusion met in the axillae, certain skin micro-organisms metabolise this secretion, forming free fatty acids and other breakdown products. These materials are odorous and responsible for 'body odour'.

The sebaceous glands are distributed over the skin surface except the palms and dorsae. They are most numerous on the scalp, forehead, face, back and chest. The secretion, sebum, consists mainly of fatty materials, wax esters, cholesterol and its esters and squalene. Normally, sebum flows freely from the glands, spreading over the skin surface. In acneic and certain other skin conditions, the sebaceous duct through which the sebum is normally secreted becomes hyperkeratinised and the opening of the duct becomes blocked. The gland

continues to produce sebum and the blocked duct distends to form a comedone. Also blocked in the duct, the (normally) commensal micro-organisms produce esterases which hydrolyse the sebum lipids, liberating free fatty acids. These fatty acids are irritant and can result in an inflammatory reaction along the wall of the duct. Leucocytes invade the inflamed area and the comedone develops into a papule and then a pustule. This is a typical acne 'spot'.

The scalp is well supplied with sebaceous glands, and the scalp, like all skin, undergoes desquamation. Due to the presence of hair, the squames tend to be retained at the scalp surface. Sebum accumulates beneath these squames and in dandruff conditions is hydrolysed by micro-organism produced esterases to form irritant fatty acids. The irritation causes proliferation of the epidermis and increased formation of the stratum corneum which again desquamates unevenly in large clumps - the dandruff scale or flake.

In our International Application No. PCT/GB37/00323 (Publication No. W087/06827) we disclosed an inhibitor of esterase-producing microorganisms in which the active ingredient comprised an aromatic acid ester of a phenol or of an aromatic alcohol, the phenol or aromatic alcohol being sufficiently water-soluble to

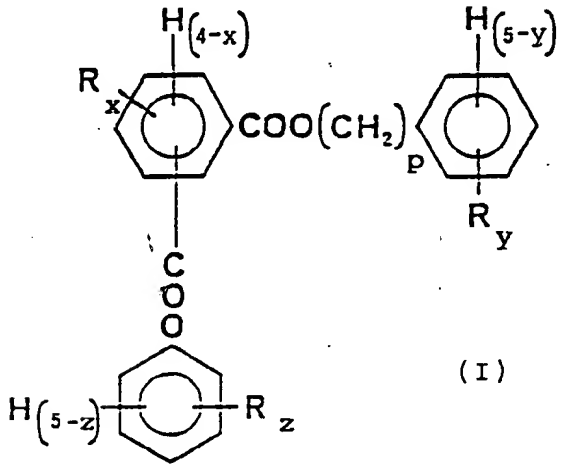
impart an anti-microbial action and the aromatic acid being sufficiently water-soluble to impart an anti-microbial action and/or to lower the pH of liquid body-secretion to a level which at least inhibits the growth of micro-organisms in the liquid body-secretions; for use in deodorants the active ingredient may be incorporated in a perfume composition which is then incorporated in a vehicle such as ethanol; for use in a dermatological composition, the active ingredient may be incorporated in an acceptable vehicle containing for example, a polyol or dimethyl suphoxide which may also act as a skin penetrant.

The effect of the active ingredient is produced by the aforementioned microbial enzymes acting to split the constituents of the ester and so hydrolyse the ester back into the aromatic acid and the phenol or aromatic alcohol. On a skin surface, such as in deodorant applications, this action occurs almost immediately but, where skin penetration is involved, as in most dermatological applications, the action is progressive.

The above term 'anti-microbial action' means an action which inhibits microbial growth, rather than one which eliminates microbial growth completely as can be achieved by a microbicide. In such skin-surface and skin-penetrating applications, the esterases produced

by the micro-organism hydrolyse a portion of the active ingredient and, in so doing, inhibit the action of the esterase and further growth of the micro-organism. After a period of time, the micro-organism may resume its metabolic activity and the above-mentioned process is repeated, and repetition will occur until the active ingredient is used up.

According to the present invention we have now found that phenyl or benzyl benzoates of the following general formula (I)



(I)

wherein R represents a hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1, and x, y and z are each 0 or an integer of from 1 to 5, are particularly effective as inhibitors of esterase-producing micro-organisms.

Benzoates of the formula (I) are hydrolysed by esterases to produce three mononuclear benzene compounds

which between them bear at least two hydroxyl substituents and two carboxyl substituents. (The hydrolysis of benzyl 4-benzoyloxybenzoate and phenyl 2-benzoyloxybenzoate are shown in Figs 1 and 2, respectively, of the accompanying drawings.) The hydrolysis products are thus highly active in performing the previously-mentioned antimicrobial and pH-lowering functions, but not to the extent of being bacteriocidal as are most conventional deodorants: not only is the elimination of cutaneous flora medically undesirable, but the use of some conventional deodorants has caused adverse reactions. Moreover, the benzoates (I) afford the further advantages of being completely odourless and non-irritant.

Preferred benzoates (I) are those in which p equals 0 or 1; and x, y and z are each zero. Such compounds have the advantage of being easy to manufacture from cheap starting materials, although the 4-benzoyloxybenzoates are preferred from the point of view of easy purification, being solids and therefore easy to crystallize. Such unsubstituted benzoates (I) have the further advantage of being generally more soluble than compounds having substituted nuclei.

Although the presence of hydroxyl substituents on the nuclei of the parent molecule increases its solubility in water, such hydroxyl substitution can lead

to increased toxic effects, and is therefore generally less preferred: and although the presence of halogen substituents increases the activity of the hydrolysis products, such halogen substitution can again lead to increased toxic effects and is also less preferred. As the 2-benzoyloxybenzoates of the general formula (I) yield a salicylic acid among their hydrolysis products, which can have an irritant effect, and the presence of a group at the 2-position can give rise to instability because of steric hindrance, and as the 3-benzoyloxy-benzoates are more expensive to produce, the 4-benzoyloxy-benzoates are generally preferred.

The primary use of benzoates (I) is as the active ingredient in a personal deodorant composition. For such an application the benzoate is first dissolved in, preferably, a perfume to form a perfume concentrate containing 5% to 50%, preferably say 10% benzoate, which is then added in an amount of about 1% to 2% to a suitable vehicle, for example ethyl alcohol, to form a deodorant composition in which the active ingredient is present in an amount of 0.1% to 0.2% and which is suitable for application by aerosol or mechanical spray.

A further use of the benzoates (1) is in the treatment of dandruff and acne where decomposition of the skin fats causes irritation. To prepare a skin

lotion, for the treatment of acne, between 0.5% and 20%, and preferably about 5%, of active ingredient is incorporated in a vehicle which may be composed of dimethyl sulphoxide, polyol, ethanol and water in suitable proportions. Anti-inflammatory substances such as hydrocortisone or glycyrrhetic acid and healing agents such as allantoin, may also be incorporated in the end product.

As a scalp lotion for the treatment of dandruff, active ingredient within the above percentages is incorporated in a hydro-alcoholic vehicle, using solubilising agents as necessary.

As a powder for the treatment of tinea pedis and foot odour, active ingredient (if liquid), within the above percentages, is adsorbed onto amorphous silica powder or light magnesium carbonate which is then mixed with say 50% talcum, starch or other suitable powder. If the active ingredient is solid, usually crystalline, the crystals are finely ground, for example in a micronniser, and then mixed with say 50% talcum, starch or other suitable powder.

Suitable perfume compositions may also be incorporated in the scalp/skin lotions and foot powders.

The skin and scalp lotions may be supplied in

sprinkler bottles for application to the scalp or the affected skin area in the form of liquid droplets which are massaged into the scalp/skin. Alternatively, the lotion may be applied by means of a pad or compress which is pre-impregnated and supplied in a sealed package; the pad is partially exposed and then applied to an affected skin area, at least once per day. In further alternative forms, the inhibitors for use in treating the scalp or skin may comprise ointments, gels, creams, lotions, sprays or powders.

The inhibitors for foot treatment are preferably in powder form, as indicated above, but might also be supplied as liquids or in sprays etc.

An example of the preparation of what is believed to be the most soluble and active ingredient for use in the above compositions will now be described.

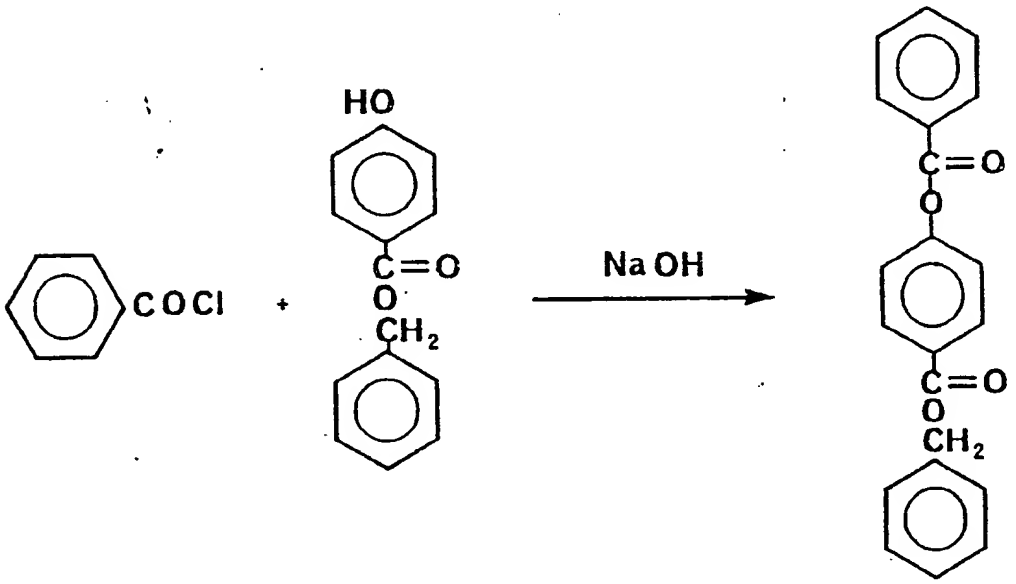
EXAMPLE

Preparation of Benzyl - 4-benzoyloxybenzoate

0.5 mol (114 g) of benzyl 4-hydroxybenzoate was dissolved in 500 mol of 5% sodium hydroxide solution. 0.51 mol (72 g) of benzoyl chloride was then added with rapid stirring. The reaction began almost immediately accompanied by a rise in temperature.

The reaction was completed in about 30 minutes when the odour of benzoyl chloride had disappeared and benzyl 4-benzoyloxybenzoate had precipitated as a fine powder or dense oil. The reaction mixture was then cooled and the aqueous liquid decanted. The reaction product was washed with water until the washings were neutral, and then filtered. Finally the crude product was recrystallized from hot 80% ethanol.

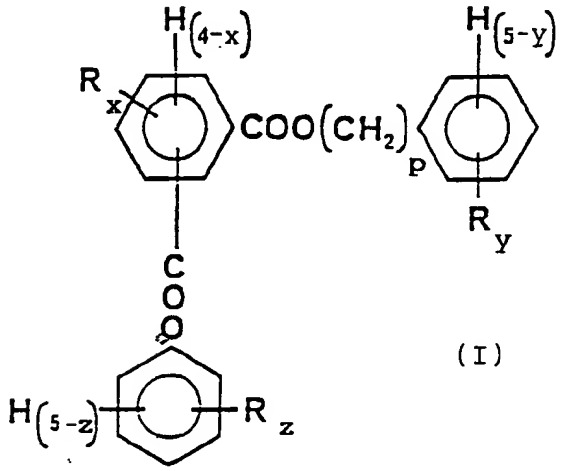
The reaction scheme may be represented as follows:



It will be appreciated that all the substituted products may be prepared by this general method.

CLAIMS:

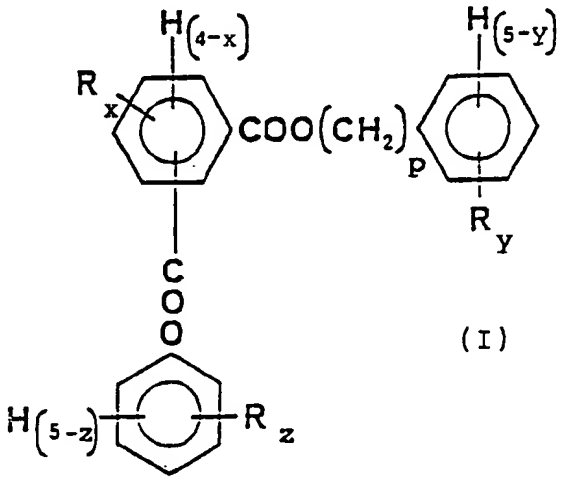
1. A deodorant composition comprising, as active ingredient, an aromatic benzoate of the following general formula (I):



(I)

wherein R represents a hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1, and x, y and z are each 0 or an integer of from 1 to 5, and a vehicle.

2. A dermatological composition comprising as active ingredient an aromatic benzoate of the general formula (I):



(I)

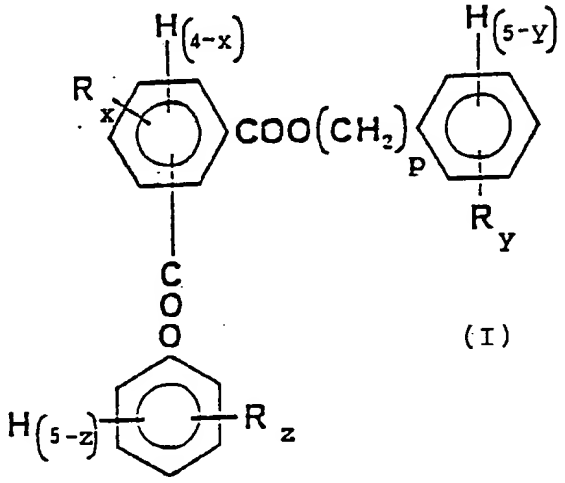
wherein R represents a hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1, and x, y and z are each 0 or an integer of from 1 to 5, and a vehicle.

3. A composition as claimed in claim 1 or 2 and additionally comprising a perfume composition.

4. A composition as claimed in claim 1, 2 or 3 wherein the aromatic benzoate is of the general formula (I) in which p = 0 or 1.

5. A composition as claimed in any preceding claim wherein the aromatic benzoate of the general formula (I) is a 4-benzoyloxy-benzoate.

6. An aromatic benzoate for use as an inhibitor of esterase-producing micro-organisms, the benzoate of the following general formula (I):



(I)

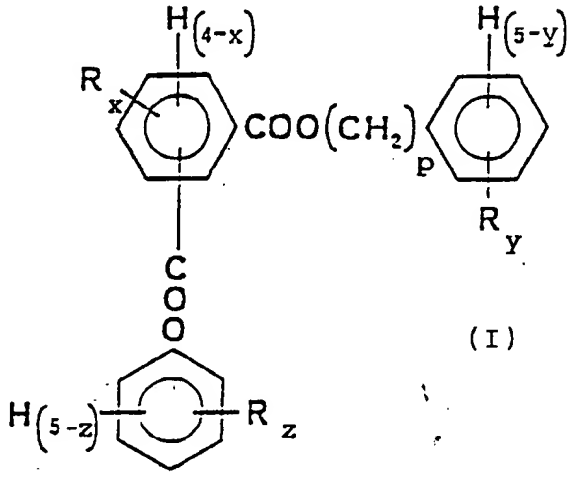
wherein R represents hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1,

and x, y and z are each 0 or an integer of from 1 to 5.

7. A benzoate as claimed in claim 6 for use as a personal deodorant.

8. A benzoate as claimed in claim 6 for use as a dermatological agent.

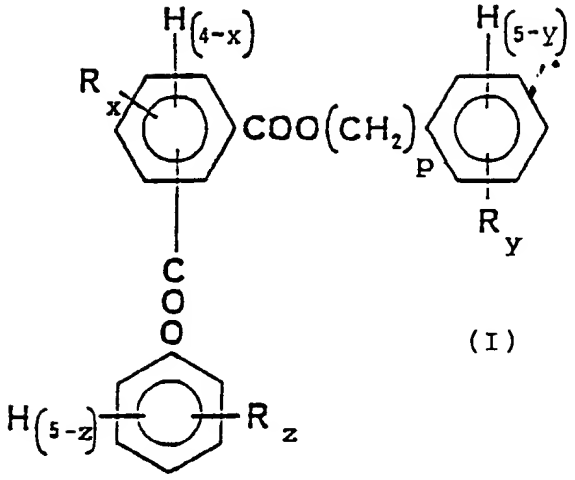
9. Use as a personal deodorant of an aromatic benzoate of the following general formula (I):



(I)

wherein R represents a hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1, and x, y and z are each 0 or an integer of from 1 to 5.

10. Use in the manufacture of a medicament for treating dermatological conditions of an aromatic benzoate of the following general formula (I):



(I)

wherein R represents a hydrogen or halogen atom or a C_{1-4} alkyl, methoxy, ethoxy or acyloxy group, p is 0 or 1, and x, y and z are each 0 or an integer of from 1 to 5.

11. Use as claimed in claim 9 or 10 of an aromatic benzoate of the general formula (I) in which p = 0 or 1.

12. Use as claimed in claim 9 or 10 of an aromatic benzoate of general formula (I), being a 4-benzoyloxy-benzoate.

FIG. 1

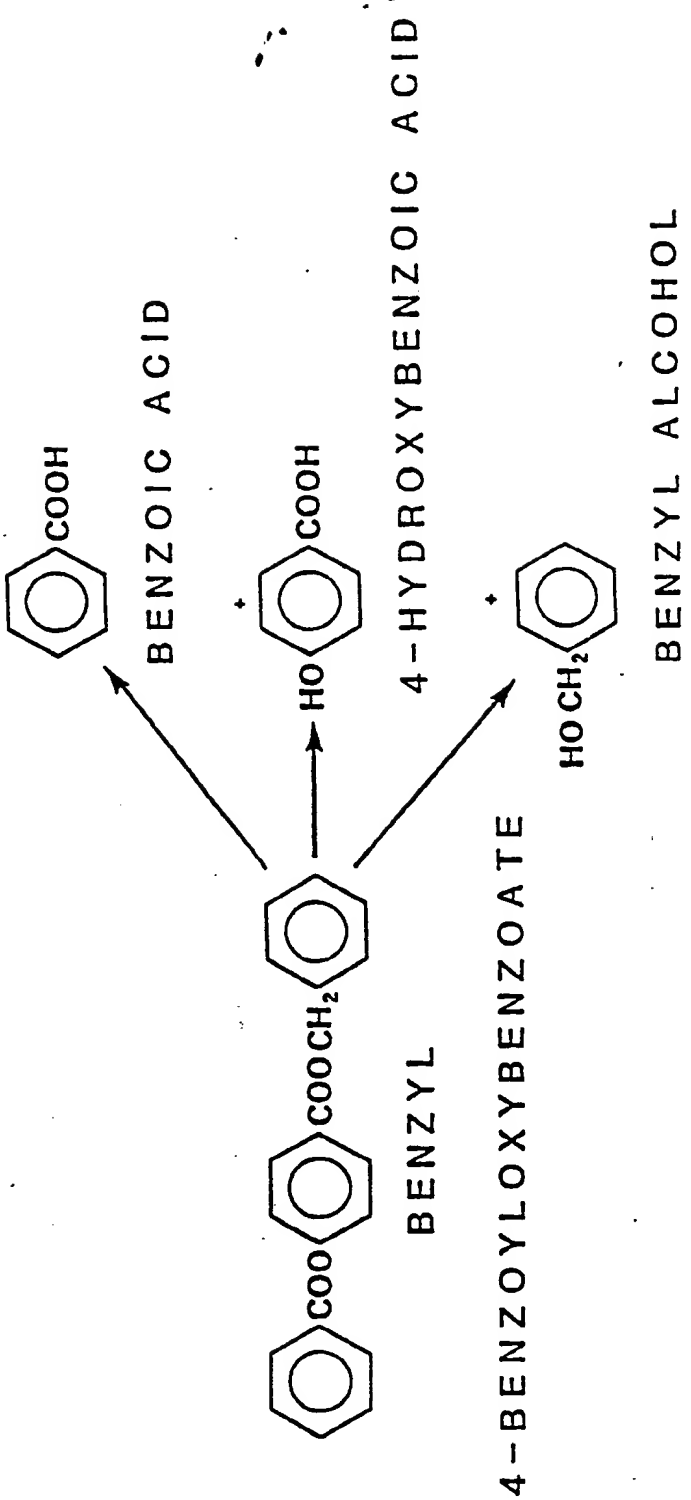
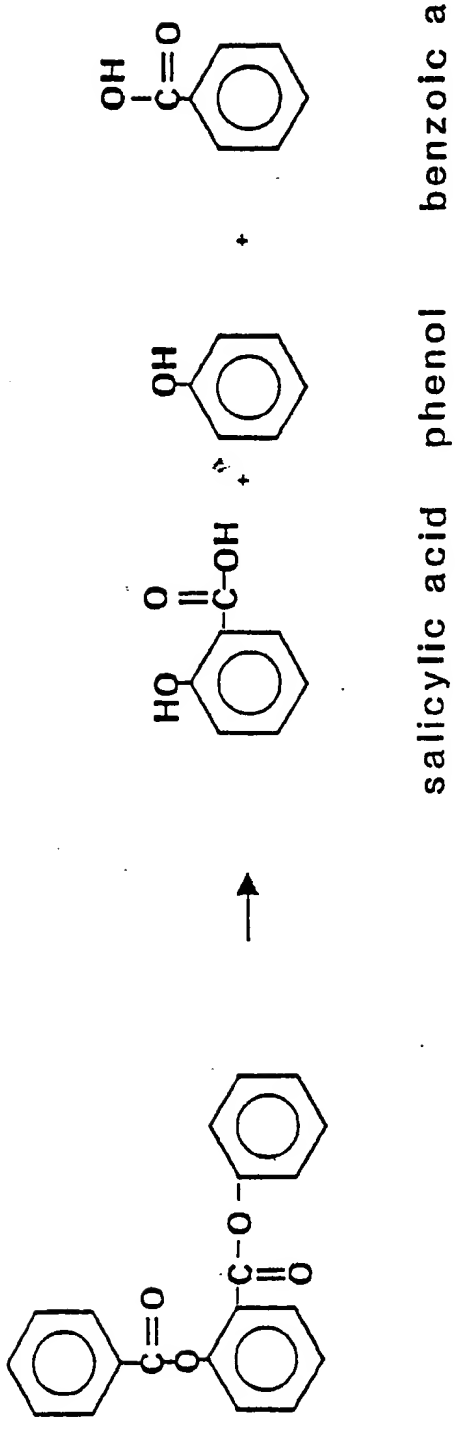

BENZOIC ACID
4-HYDROXYBENZOIC ACID
BENZYL ALCOHOL
4-BENZOYLOXYBENZOATE
BENZYL
COOH
HO
HO CH2
COO
COOCH2

FIG. 2



INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 90/01750

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[5]: A 61 K 7/32, 7/48, 91/235

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	A 61 K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	FR, A, 2108219 (SYNVAR ASSOCIATES) 19 May 1972 see page 8; page 24, example G; pages 37,38; claims 1,2,9 --	2,4,10,11
A	WO, A, 87/06827 (ROBERTET S.A.) 19 November 1987 see page 4, line 8 - page 6, line 10; claims (cited in the application) --	1,2,5,6,9,10
A	STN File supplier (Karlsruhe, DE) Chemical Abstracts, vol. 80, no. 25, abstract 145799d, & JP, A, 49006898 (SHIONOGI & CO.) 16 February 1974, see abstract --	1,2,4-12
A	WO, A, 85/03289 (YOSHITOMI PHARMACEUTICAL IND.) 1 August 1985 see page 1, formula I; claim 1 --	1,2,4-12

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
14th February 1991	07. 03. 91
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	p.p. MISS D. S. KOWALCZYK

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, ** with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	Patent Abstracts of Japan, vol. 10, no. 56 (C-331)(2113), 6 March 1986 & JP, A, 60199859 (YOSHITOMI SEIYAKU K.K.) 9 October 1985, see abstract	1,2,4-12

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9001750 SA 41745

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on 04/03/91
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A- 2108219	19-05-72	AU-A- 3326071	15-03-73
		DE-A- 2144963	31-05-72
WO-A- 8706827	19-11-87	AU-A- 7395487	01-12-87
		EP-A- 0307400	22-03-89
		JP-T- 1502907	05-10-89
		ZA-A- 8703425	03-11-87
WO-A- 8503289	01-08-85	JP-A- 60156646	16-08-85
		EP-A- 0169246	29-01-86